Gall bladder contractility in preterm infants

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Abstract
Postnatal response of the gall bladder to feeding was studied in 28 preterm infants (gestational age 24–37 weeks) by ultrasonography immediately before feeding and one hour after feeding. Nineteen of the infants were studied once during the first week of life, and nine infants were studied weekly from a postconceptional age of 27–31 until a postprandial gall bladder contraction was seen. A contraction index was calculated as a percentage decrement of the surface area of the gall bladder from its initial value.

All preterm infants of more than 33 weeks’ gestation showed a gall bladder response to feeding with a contraction index of at least 50%. Very preterm infants (gestational age 27–32 weeks) showed no postprandial gall bladder contraction or the contraction index was under 50%. In a follow up study of nine very preterm infants, the contraction index exceeded 50% at a postconceptional age of 29 to 32 weeks. One infant with prolonged feeding problems had no postprandial gall bladder response before the postconceptional age of 38 weeks. The contraction index increase was dependent on gestational age at birth and on the bolus volume of feeds.

(Arch Dis Child 1993;68:43–5)

The development of gastrointestinal function depends on integrated maturation of digestive, absorptive, and motor function. Intolerance to enteral feeding is common in preterm infants, and the nutritional requirements of very preterm infants cannot always be met with enteral feeding.

Malabsorption of fat is particularly common in premature infants. Postprandial gall bladder contraction is necessary for establishment of an adequate bile acid concentration in the intestine to form the micellar solution that enhances fat absorption. Cholecystokinin (CCK) plays an important part in regulating basal gall bladder tone and postprandial gall bladder contraction. CCK secretion is stimulated by fat, protein, and amino acids, and, to a lesser degree, by glucose.

A clear gestationally dependent schedule can be seen in the development of fasting intestinal motility in preterm infants. It is probably related to the maturation of the intrinsic enteric neural network. The development of postprandial intestinal activity is mainly determined by the duration of enteral feeding and the increase of feed volume. In contrast to fasting motility, postconceptional age is not an important determinant of the development of postprandial motility.

The present study was conducted on the development schedule of postprandial gall bladder contractility and associated factors in preterm infants.

Subjects and methods
In the first part of the study, gall bladder contractility was measured in 19 preterm infants (gestational age 27–35 weeks) at a postnatal age of 1–6 days when they began to tolerate a 10 ml bolus of breast milk. In the second part of the study, nine infants born at 24–31 weeks’ gestation were studied weekly until a clear postprandial contraction response of the gall bladder was detected. The infants were examined immediately before and one hour after feeding. The feeding interval was three hours. Enteral feeding with small amounts of breast milk was started during the first three days of life in all infants. The volume of feed was increased as the infant’s tolerance to feeds increased.

Ultrasound examinations of the biliary tract were carried out using an Aloka Echocamera SSD-500 equipped with a 5MHz convex probe (Aloka UST 935N-S). The planimetric ellipsoid size of the gall bladder was measured on the basis of its maximal longitudinal ultrasonographic image (fig 1). The image of the gall bladder was documented using an Aloka Echo Copier SSD-300S. The contraction index of the gall bladder was calculated as a percentage decrement of the surface area from its initial value (contraction index=fasting gall bladder size/postprandial gall bladder size)/fasting gall bladder size ×100%). The diameter of the common bile duct was also measured.

The maximum surface area of the gall bladder was measured twice. The method error as a percentage of the mean of the surface area was 10-7%.

Multiple linear regression analysis was used to study the relationship between contraction index and gestational age, postconceptional age, duration of enteral feeding, or bolus volume of feeds.

The study design was approved by the joint committee on ethics of Turku University and the Turku University Central Hospital. Informed consent was obtained from parents.
Results
During the first part of the study all preterm infants with a gestational age of more than 32 weeks (n=8) showed a clear postprandial gall bladder contraction (contraction index >50%) when the feeding interval was three hours. In more immature infants (gestational age 27 to 32 weeks, n=11), the gall bladder was not visualised (n=6) during feeding intervals or the contraction was only partial (contraction index <50%, n=3) or absent (n=2) (fig 2).

In a follow up study of nine very preterm infants with a gestational age of 24–31 weeks, the maturation of gall bladder contractility was further studied during bolus feeding, which was carried out as tolerated by the individual infant. Bolus volume was recorded. The contraction index was initially zero or less (that is, gall bladder size increased after the meal) in most infants, and increased to 50–100% during the first five postnatal weeks, corresponding to a postconceptional age of 28 to 32 weeks. The only exception was an infant with a severe feeding problem whose contraction index was more than 50% only after a postnatal age of 10 weeks (postconceptional age of 38 weeks) (fig 3).

Using the contraction index as the dependent factor and bolus volume, gestational age, postconceptional age, and duration of enteral feeding as predictor factors, multiple linear regression analyses yielded a multiple correlation coefficient of 0.66. Bolus volume and gestational age were the only variables significantly related to contraction index (p<0.0001 and 0.01, respectively).

The diameter of the common bile duct was less than 2 mm in all infants, and it remained unchanged after gall bladder contraction. No sludge was seen in any gall bladder.

Discussion
In this study, a gestational age of 32 weeks was clearly a turning point in the maturation of gall bladder contraction. A clear contraction was seen in the older infants, whereas the younger ones still showed immature function of the gall bladder. This is in agreement with the clinical observation that nutritional requirements of preterm infants with a gestational age of more than 32 weeks can be met with enteral feeds.

The development of postprandial gall bladder contraction in very preterm infants was dependent on gestational age, but the most
important determinant of the response of the gall bladder was the bolus volume of the feed. Postnatal age, postconceptional age, and duration of enteral feeding were not important for the maturation of gall bladder contractility. Bolus volume, however, is dependent on the clinical condition of the child. Those infants in good condition were given larger volumes earlier.

Feed volume is also an important determinant of the development of postprandial motor activity of the intestine. This activity and gall bladder contraction are hormonally mediated; the induction of postprandial motor activity is associated with the release of intestinal polypeptides such as gastrin, CCK, and peptide YY,

and gall bladder contraction is regulated by CCK.

CCK secretion already occurs during the second trimester, and the amount of CCK in the human fetal mucosa is only slightly increased during the third trimester. The postprandial hormonal response might, however, be weaker. The postprandial responses to the first feeding of such hormones as plasma insulin, growth hormone, pancreatic glucagon, and enteroglucagon have been found to be weaker in preterm infants.

In one infant, delayed maturation of gall bladder contractility was associated with a severe feeding problem due to very slow passage. Because no defined aetiology was found, it was not possible to state any causal conclusion, but the example suggests a close relationship between gall bladder contractility and postprandial motor function of the intestine.

In conclusion, the development of postprandial gall bladder contractility in preterm infants was found to be dependent on gestational age with a maturational turning point of 32 weeks' gestation. Additionally the bolus volume of feeds was also an important determinant of gall bladder contractility.

This study was financially supported by the Foundation for Gastroenterological Research and the Finnish Paediatric Research Foundation.